REMARKS

Claims 14-18 were under examination in the outstanding Office Action dated March 25, 2003. Claims 1-13 and 19-22 have been withdrawn from consideration by the Examiner as drawn to a non-elected invention. Applicants have amended Claims 14-18 and have added new Claims 56-63, which are similar to original Claims 2-9, except that new Claims 56-64 depend from Claim 14 rather than Claim 1.

Claims 14-18 stand rejected for indefiniteness and for lack of novelty or obviousness over the art. The issues raised in the Office Action will be addressed individually below.

I. Restriction Requirement.

Applicants again respectfully request reconsideration of the Restriction Requirement with respect to Groups I and II. The method of Claim 14 (Group II) recites use of the antibody of Claim 1 (Group I). Accordingly, Groups I and II are directed to a product and methods of use thereof. It is therefore requested that the outstanding Restriction Requirement be reconsidered and the claims of Group I (Claims 1-13) subject to substantive examination.

II. Indefiniteness.

Claims 14-18 stand rejected under 35 U.S.C. § 112, second paragraph for indefiniteness. First, Claim 14 stands rejected as indefinite for depending from withdrawn Claim 1. Claim 14 has been amended to independent form and to incorporate the recitations of Claim 1.

In addition, Claims 15-18 stand rejected for reciting "a" method according to Claim 14. Claims 15-18 have been amended to recite "the" method as suggested by the Examiner.

Applicants note for the record that these claim amendments do not alter the scope of the claims.

In view of the foregoing, Applicants submit that Claims 14-18 satisfy the requirements of §112, second paragraph and respectfully request that the rejections on this basis be withdrawn.

III. The Claims are Novel over Lewis et al.

Claims 14-16 and 18 stand rejected under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 5,049,656 (Lewis et al.). The Office Action states that "Lewis et al. teach using antibody specifically recognized impurities, i.e. capping oligonucleotides (covalent bound), for polypeptide or oligonucleotides synthesis process," citing Col. 5, lines 35-45 of the Lewis et al. patent. Applicants respectfully disagree that Lewis et al. anticipates the claimed invention.

The Lewis et al. patent is concerned with the problem of contamination of synthetic peptides or oligonucleotides by incomplete molecules which are generated the synthesis reaction. Lewis et al. describes a method for separating the contaminating incomplete molecules (termed "failed" peptides and oligonucleotides by Lewis et al.) from the desired end-product (*i.e.*, the full-length peptide or oligonucleotide). With respect to oligonucleotides, Lewis et al. teaches that the failed oligonucleotides can be separated from the full-length oligonucleotides by reacting the mixture with a capping agent that specifically modifies the failed oligonucleotides (*see*, Col. 7, line 20 to Col. 8, line 23). The capping agent is recognized by an antibody, which can be used to selectively separate the capped failed oligonucleotides from the uncapped full-length oligonucleotides. In an alternative "reverse" method, the capping agent specifically recognizes the desired full-length oligonucleotide, but does not react with the failed oligonucleotides (Col. 7, lines 33-35 and Col. 8, lines 12-23). In this case, the antibody will bind to the capped full-length oligonucleotides, which can thereby be separated from the failed uncapped oligonucleotides.

Thus, according to the methods of Lewis et al., contaminating failed oligonucleotides can be labeled and selectively removed from the mixture by

reaction with an antibody that recognizes the capping agent (or, in the "reverse" method, the desired full-length oligonucleotide is labeled and recognized by the antibody).

In contrast, the presently-claimed invention is directed to methods of detecting incompletely deprotected synthetic oligonucleotides. According to the methods of the invention, a synthetic oligonucleotide is contacted with an antibody. The antibody specifically binds to a synthetic oligonucleotide that is modified by an organic protecting group covalently bound thereto, but does not bind to the unmodified synthetic oligonucleotide (*i.e.*, not covalently bound to the organic protecting group). The presence or absence of antibody binding to the synthetic oligonucleotide is detected, with the presence of binding indicating that the synthetic oligonucleotide is incompletely deprotected.

Lewis et al. can be clearly distinguished from the presently-claimed methods. For example, Lewis et al. is only concerned with the removal of failed (*i.e.*, incomplete or truncated) oligonucleotides. Unlike the present invention, the Lewis et al. reference does not disclose or in any way suggest a method of detecting incompletely deprotected synthetic oligonucleotides. Indeed, it is not possible using the method of Lewis et al. to detect incompletely deprotected oligonucleotides as accomplished by the present inventors. Further, the capping agent of Lewis et al. is not an "organic protecting group" and the antibodies of Lewis et al. do not "specifically bind[s] to a synthetic oligonucleotide having an organic protecting group covalently bound thereto" as recited by the present claims.

In addition, the Lewis et al. patent requires the introduction of an artificial capping molecule that is not part of the normal synthetic chemistry into the reaction mixture. In contrast, according to the present invention, it is not necessary to add a cap or other label to the unwanted contaminating oligonucleotides to permit detection thereof.

In view of the foregoing, it is clear that Lewis et al. does not disclose or even suggest the methods of the present invention. Accordingly, the

presently-claimed invention is both novel and unobvious over this reference, and the Applicants respectfully request withdrawal of the rejection under §102(b).

IV. The Claimed Subject Matter is Unobvious over Lewis et al. in view of Tortora et al.

Claim 17 stands rejected under 35 U.S.C. § 103 for obviousness over Lewis et al., as applied above, in view of Tortora et al. (Microbiology 6th edition (1997), page 497). The Office Action concedes that Lewis et al. does not teach using a sandwich assay, but argues that sandwich assays are well-known in the art, citing a sandwich ELISA assay described by Tortora et al. The Lewis et al. patent has been addressed in the preceding section. The deficiencies of Lewis et al. are not remedied by combination with Tortora et al. Neither of the cited references, alone or in combination, discloses or suggests a method of detecting incomplete deprotection of a synthetic oligonucleotide as accomplished by the present inventors. Further, neither of these references discloses or provides any suggestion of an antibody that specifically binds to "an organic protecting group" and thereby detects incompletely deprotected synthetic oligonucleotides as recited by the present claims.

In view of the foregoing, Applicants submit that the subject matter of the present claims is not rendered obvious by Lewis et al. in combination with Tortora et al., and respectfully request that the rejection on this basis be withdrawn.

V. Conclusion.

The points and concerns raised in the outstanding Office Action having been addressed in full, it is submitted that this application is in condition for allowance, which action is respectfully requested.

Respectfully submitted,

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